CLAIMS

1. A method of [^{11}C]-radiolabelling a phenothiazine compound or a phenothiazine-like compound, wherein:

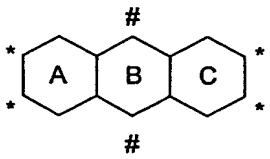
said compound has a polycyclic core of three six-membered rings fused together in a linear fashion and denoted the A-ring, B-ring, and C-ring, where the B-ring is the "middle" ring;

said polycyclic core is partially-aromatic or fully-aromatic;

said polycyclic core has 14 ring atoms, including exactly 1 or exactly 2 ring heteroatom(s), each of which is independently selected from N, O, and S;

the remainder of said ring atoms being C;

said exactly 1 or exactly 2 ring heteroatom(s) form part of the B-ring, but not part of the A-ring or C-ring, and so are located at one or both of the "central" positions denoted by a hash-mark (#) in the following depiction of the polycyclic core:



said compound has a pendant group covalently attached to a ring atom of said polycyclic core;

said pendant group is independently:

a primary amino group;

a cationic primary imino group;

a secondary amino group;

a cationic secondary imino group;

a primary imino group; or

a secondary imino group;

said method comprising the step of:

reacting said phenothiazine compound or a phenothiazine-like compound with [^{11}C]methyl trifluoromethanesulfonate ($CF_3SO_2O^{11}CH_3$);

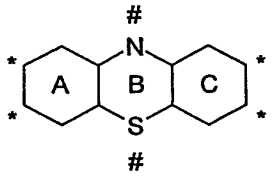
thereby converting said pendant group to a corresponding [^{11}C]methyl-labelled pendant group, respectively:

a [^{11}C]methyl-labelled secondary amino group;
a [^{11}C]methyl-labelled cationic secondary imino group;
a [^{11}C]methyl-labelled tertiary amino group;
a [^{11}C]methyl-labelled cationic tertiary imino group;
a [^{11}C]methyl-labelled secondary imino group; or
a [^{11}C]methyl-labelled cationic tertiary imino group;

to give a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.

2. A method according to claim 1, wherein said polycyclic core has 14 ring atoms, including exactly 2 ring heteroatoms, each of which is independently selected from N, O, and S.

3. A method according to claim 1, wherein said polycyclic core has 14 ring atoms, including exactly 2 ring heteroatoms: N and S:



4. A method according to any one of claims 1 to 3, wherein said polycyclic core is fully-aromatic.

5. A method according to any one of claims 1 to 4, wherein said pendant group is independently attached to a ring carbon atom of said polycyclic core.

6. A method according to any one of claims 1 to 4, wherein said pendant group is independently attached to a ring carbon atom of said A-ring or C-ring, but not of said B-ring.

7. A method according to any one of claims 1 to 4, wherein said pendant group is independently attached at one of the "distal" positions of said A-ring or C-ring, which positions are denoted by asterisks (*).

8. A method according to any one of claims 1 to 7, wherein said pendant group is independently:

a secondary amino group or

a cationic secondary imino group;

and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is:

a [^{11}C]methyl-labelled tertiary amino group; or

a [^{11}C]methyl-labelled cationic tertiary imino group.

9. A method according to any one of claims 1 to 7, wherein said pendant group is independently selected from:

$-NH_2$, $-NHR$, $=N^{(+)}H_2$, $=N^{(+)}HR$, $=NH$, and $=NR$;

wherein R is independently selected from C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, C_{1-6}cycloalkyl, and C_{1-6}cycloalkenyl, and is optionally substituted with one or more groups selected from halo (e.g., fluoro, chloro, bromo, iodo), hydroxy, and C_{1-4}alkoxy;

and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is:

$-NH-(^{11}CH_3)$, $-NR-(^{11}CH_3)$, $=N^{(+)}H-(^{11}CH_3)$, $=N^{(+)}R-(^{11}CH_3)$, or $=N-(^{11}CH_3)$.

10. A method according to any one of claims 1 to 7, wherein said pendant group is independently selected from: $-NHR$ and $=N^{(+)}HR$;

wherein R is independently selected from C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, C_{1-6}cycloalkyl, and C_{1-6}cycloalkenyl, and is optionally substituted with one or more groups selected from halo (e.g., fluoro, chloro, bromo, iodo), hydroxy, and C_{1-4}alkoxy;

and said corresponding [^{11}C]methyl-labelled pendant group, respectively, is: $-NR-(^{11}CH_3)$ or $=N^{(+)}R-(^{11}CH_3)$.

11. A method according to claim 9 or 10, wherein R is independently C_{1-4}alkyl.

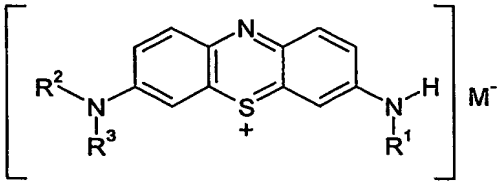
12. A method according to claim 9 or 10, wherein R is independently -Me or -Et.

13. A method according to claim 9 or 10, wherein R is independently -Me.

14. A method according any one of claims 1 to 13, wherein said compound has, in addition to said pendant group, one or more additional substituents selected from:

amino ($-NH_2$), methylamino (-NHMe), dimethylamino ($-NMe_2$), ethylamino (-NHEt), diethylamino ($-NEt_2$), imino (=NH), methylimino (=NMe), ethylimino (=NEt), methyl (-Me), ethyl (-Et), fluoro (-F), chloro (-Cl), bromo (-Br), iodo (-I), oxo (=O), hydroxy (-OH), carboxy (-COOH), and protonated and deprotonated forms thereof.

15. A method according to claim 1, wherein the phenothiazine or phenothiazine-like compound is a compound of the following formula:



wherein:

each of R^1, R^2, and R^3 is independently -H, C_{1-6}alkyl, C_{1-6}alkenyl, C_{1-6}alkynyl, C_{1-6}cycloalkyl, and C_{1-6}cycloalkenyl, and is optionally substituted with one or more groups selected from halo (e.g., fluoro, chloro, bromo, iodo), hydroxy, and C_{1-4}alkoxy; and

M^- is an anion.

16. A method according to claim 15, wherein $-NHR^1$ is independently -NHMe.

17. A method according to claim 15 or 16, wherein $-NR^2R^3$ is independently $-NH_2$.

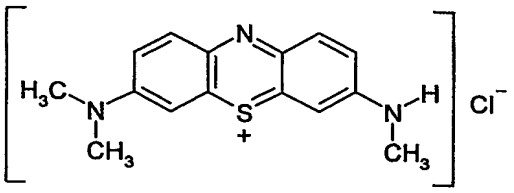
18. A method according to claim 15 or 16, wherein $-NR^2R^3$ is independently -NHMe.

19. A method according to claim 15 or 16, wherein $-NR^2R^3$ is independently $-NMe_2$.

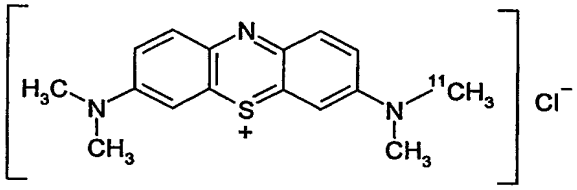
20. A method according to any one of claims 15 to 19, wherein M^- is independently a halide ion.

21. A method according to any one of claims 15 to 19, wherein M^- is independently Cl^-.

22. A method according to claim 1, wherein the phenothiazine or phenothiazine-like compound is Azure B:



and said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound is [N-methyl-^{11}C]methylene blue:



23. A method according to any one of claims 1 to 22, wherein said reaction is performed in the presence of a Bronsted base.

24. A method according to any one of claims 1 to 22, wherein said reaction is performed in the presence of an alkali metal carbonate or bicarbonate.

25. A method according to any one of claims 1 to 22, wherein said reaction is performed in the presence of potassium carbonate (K_2CO_3).

26. A method according to any one of claims 1 to 25, wherein said reaction is carried out in aqueous media.

27. A method according to any one of claims 1 to 25, wherein said reaction is carried out by introducing said [^{11}C]methyl trifluoromethanesulfonate into an aqueous solution or suspension of said phenothiazine or phenothiazine-like compound, to form a reaction mixture.

28. A method according to claim 27, wherein said aqueous solution or suspension further comprises a Bronsted base.

29. A method according to claim 27, wherein said aqueous solution or suspension further comprises an alkali metal carbonate or bicarbonate.

30. A method according to claim 27, wherein said aqueous solution or suspension further comprises potassium carbonate (K_2CO_3).

31. A method according to any one of claims 27 to 30, wherein said reaction mixture is mixed for a mixing time of 1-30 minutes.

32. A method according to any one of claims 27 to 30, wherein said reaction mixture is mixed for a mixing time of 1-10 minutes.

33. A method according to any one of claims 27 to 32, wherein said reaction is carried out at 20°C-25°C.

34. A method according to any one of claims 27 to 32, wherein said reaction is carried out under an inert atmosphere.

35. A method according to any one of claims 27 to 32, wherein said reaction is carried out under argon.

36. A method according to any one of claims 1 to 35, further comprising the subsequent step of:

purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.

37. A method according to any one of claims 1 to 35, further comprising the subsequent step of:

purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using ion exchange methods.

38. A method according to any one of claims 1 to 35, further comprising the subsequent step of:

purifying said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using cation exchange methods.

39. A method according to any one of claims 1 to 38, wherein the reaction and optional purification is performed in less than 60 minutes.

40. A method according to any one of claims 1 to 38, wherein the reaction and optional purification is performed in less than 45 minutes.

41. A method according to any one of claims 1 to 38, wherein the reaction and optional purification is performed in less than 40 minutes.

42. A method according to any one of claims 1 to 41, which provides a radiochemical purity greater than 90%.

43. A method according to any one of claims 1 to 42, which provides a radiochemical yield of at least 2%.

44. A method according to any one of claims 1 to 43, which provides a specific average activity of at least 0.5 GBq/μmol.

45. A method according to any one of claims 1 to 44, which is partially or fully automated.

46. A [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound which is *obtained* by a method as defined in any one of claims 1 to 45.

47. A composition comprising a compound according to claim 46.

48. A composition comprising a compound according to claim 46 and a pharmaceutically acceptable carrier or excipient.

49. A method of PET imaging which employs a compound according to claim 46.

50. A method of PET imaging comprising the steps of:

(i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to any one of claims 1 to 45;

(ii) introducing said compound into a subject; and

(iii) PET imaging (e.g., a part of, the whole of) the subject.

51. A compound according to claim 46 for use in a method of treatment of the human or animal body by therapy.

52. A compound according to claim 46 for use in a diagnostic or prognostic method practiced on the human or animal body.

53. Use of a compound according to claim 46 in the manufacture of a medicament for use in the treatment of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease).

54. Use of a compound according to claim 46 in the manufacture of a medicament (e.g., a diagnostic or prognostic reagent) for use in the diagnosis or prognosis of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease).

55. Use of:

(i) a phenothiazine compound or a phenothiazine-like compound, wherein:

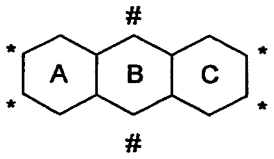
said compound has a polycyclic core of three six-membered rings fused together in a linear fashion and denoted the A-ring, B-ring, and C-ring, where the B-ring is the "middle" ring;

said polycyclic core is partially-aromatic or fully-aromatic;

said polycyclic core has 14 ring atoms, including exactly 1 or exactly 2 ring heteroatom(s), each of which is independently selected from N, O, and S;

the remainder of said ring atoms being C;

said exactly 1 or exactly 2 ring heteroatom(s) form part of the B-ring, but not part of the A-ring or C-ring, and so are located at one or both of the "central" positions denoted by a hash-mark (#) in the following depiction of the polycyclic core:



said compound has a pendant group covalently attached to a ring atom of said polycyclic core;

said pendant group is independently:

a primary amino group;

a cationic primary imino group;

a secondary amino group;

a cationic secondary imino group;

a primary imino group; or

a secondary imino group;

and

(ii) [^{11}C]methyl trifluoromethanesulfonate ($CF_3SO_2O^{11}CH_3$);

in the manufacture of a medicament for use in the treatment of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease).

56. Use of:

(i) a phenothiazine compound or a phenothiazine-like compound, wherein:

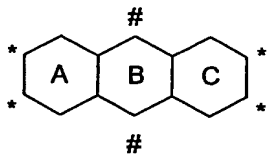
said compound has a polycyclic core of three six-membered rings fused together in a linear fashion and denoted the A-ring, B-ring, and C-ring, where the B-ring is the "middle" ring;

said polycyclic core is partially-aromatic or fully-aromatic;

said polycyclic core has 14 ring atoms, including exactly 1 or exactly 2 ring heteroatom(s), each of which is independently selected from N, O, and S;

the remainder of said ring atoms being C;

said exactly 1 or exactly 2 ring heteroatom(s) form part of the B-ring, but not part of the A-ring or C-ring, and so are located at one or both of the "central" positions denoted by a hash-mark (#) in the following depiction of the polycyclic core:



said compound has a pendant group covalently attached to a ring atom of said polycyclic core;

said pendant group is independently:

a primary amino group;

a cationic primary imino group;

a secondary amino group;

a cationic secondary imino group;

a primary imino group; or

a secondary imino group;

and

(ii) [^{11}C]methyl trifluoromethanesulfonate ($CF_3SO_2O^{11}CH_3$);

in the manufacture of a medicament (e.g., a diagnostic or prognostic reagent) for use in the diagnosis or prognosis of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease).

57. A method of manufacturing a medicament for use in the treatment of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) which includes the steps of a method according to any one of claims 1 to 45.

58. A method of manufacturing a medicament for use in the diagnosis or prognosis (e.g., of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) which includes the steps of a method according to any one of claims 1 to 45.

59. A method of treatment of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) in a patient, comprising administering to said patient a therapeutically-effective amount of a compound according to claim 46.

60. A method of treatment of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) in a patient, comprising the steps of:

(i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to any one of claims 1 to 45;

(ii) administering to said patient a therapeutically-effective amount of said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound.

61. A method of diagnosis or prognosis of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) which employs a compound according to claim 46.

62. A method of diagnosis or prognosis of skin cancer (e.g., melanoma) or a tauopathy (e.g., Alzheimer's disease) comprising the steps of:

(i) preparing a [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound using a method according to any one of claims 1 to 45;

(ii) introducing said [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound into the subject;

(ii) determining the presence and/or location and/or amount of [^{11}C]-radiolabelled phenothiazine or phenothiazine-like compound in (e.g., a part of, the whole of) the subject;

(iii) correlating the result of the determination made in (ii) with a disease condition of the subject.